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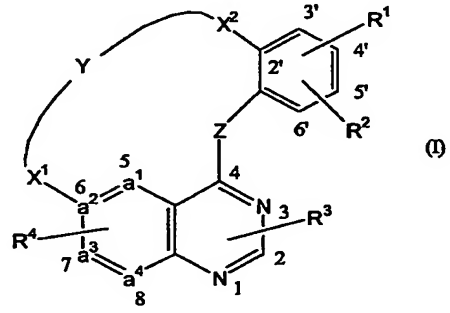
(54) Title: PYRIDO- AND PYRIMIDOPYRIMIDINE DERIVATIVES AS ANTI- PROLIFERATIVE AGENTS



(I)

(57) Abstract: The present invention concerns the compounds of formula (I) the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein a^1-a^2=a^3-a^4 represents a divalent radical selected from N-CH=CH-CH, N-CH N-CH or CH-CH=N-CH; Z represents NH; Y represents -C_{3-9}alkyl-, -C_{1-5}alkyl-NR^{13}-C_{1-5}alkyl-,-C_{1-6}alkyl-NH-CO- or -CO-NH -C_{1-6}alkyl- ; X^1 represents -O- or -NR^{11}-; X^2 represents -C_{1-2}alkyl-, -O-C_{1-2}alkyl, -O- or -O-CH_2-;R^1 represents hydrogen or halo; R^2 represents hydrogen, cyano, halo, hydroxycarbonyl-C_{1-4} alkyloxycarbonyl-, Het^{16}-carbonyl- or Ar^5; R^3 represents hydrogen; R^4 represents hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^4 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-; R^{11} represents hydrogen; R^{12} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-; R^{13}represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl; Het^2 represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C_{1-4}alkyl-, preferably methyl; Het^{14} represents morpholinyl; Het^{16} represents a heterocycle selected from morpholinyl or pyrrolidinyl; Ar^4 represents phenyl; Ar^5 represents phenyl optionally substituted with cyano.

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